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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/594,577	06/15/2000	Hideaki Hosokawa	000683	8983

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EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	6

DATE MAILED: 05/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/594,577	Applicant(s) HOSOKAWA ET AL.	
	Examiner Gary B. Nickol Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 3-12-02 .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above claim(s) 5,8-10,14,15,17 and 20-30 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4,6,7,11-13,16,18 and 19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-13, 16-22) in Paper No. 5 is acknowledged. The species election of an antibody, specifically the anti-Le^a antibody is acknowledged.

Claims 1-30 are pending.

Claims 5, 8-10, 14-15, 17, 20-30 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1-4, 6-7, 11-13, 16, 18-19 are currently pending and are under consideration.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on June 18, 1999. It is noted, however, that applicant has not filed a certified copy of the 11-172485 application as required by 35 U.S.C. 119(b).

Specification

The specification is objected to for the following reason: The specification on page 1 should be amended to reflect the priority status of the present application. Except for a continued prosecution application filed under § 1.53(d), any nonprovisional application claiming the benefit of one or more prior filed copending nonprovisional applications or international applications designating the United States of America must contain a reference to each such prior

application, identifying it by application number (consisting of the series code and serial number) or international application number and international filing date and indicating the relationship of the applications.

Claim Objections

Claims 4, and 16 are objected to because of the following informalities: Claims 4 and 16 recite "any one of Claim" as it appears the word "Claim" should be pluralized. Appropriate correction is required.

Claims 2 and 12-13 are objected to for being unclear. Claim 2 recites "measuring an amount of carcinoembryonic antigens, an antibody", and Claims 12-13 recite "measuring an amount of a complex of carcinoembryonic antigens, an antibody". These claims are unclear because there is no connection between use of the antibody and measuring the CEAs. Or- does the complex of CEAs (which is detected) comprise the antibody and protein? Clarification/amendments are requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-7, 11-13, 16, and 18-19 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 6-7, 11-13, 16, and 18-19 are rejected as vague and indefinite for reciting "modified sugar chain" as the specification does not clearly set forth what these "modifications" encompass nor does the specification define what is meant by "modified". For example, are the "modified sugar chains" on carcinoembryonic antigens different in normal versus diseased states? As written, the metes and bounds of the claims cannot be determined.

Claims 11-13, 16, 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a correlation step indicating how the amounts of CEAs detected differentiate between cancerous and normal samples (control).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, and 11-13 rejected under 35 U.S.C. 102(b) as being anticipated by Nagata *et al.* (Tumor Biol., 1991, Vol. 12, pages 35-44, IDS).

The claims are broadly drawn to a method for detection of carcinoembryonic antigens (CEAs) (and or a complex of CEAs) having a modified sugar chain structure which comprises using an antibody against a constant region of CEAs and a protein capable of recognizing a modified sugar chain structure of CEA (Claims 1 and 2). The claims are further drawn to a method for detection of CEAs having a modified sugar chain structure which comprises reacting

a sample with an antibody against a common region of CEAs and a protein capable of recognizing a modified sugar chain structure of CEAs to give a complex of CEAs, the specific antibody and the protein, and measuring an amount of the complex (Claim 3).

The claims are further drawn to a method for detecting a cancer which comprises using an amount of CEAs having a modified sugar chain structure as an indicator for the detection (Claim 11); A method for detecting a cancer which comprises measuring a complex of CEAs, an antibody against a common region of CEAs and a protein capable of recognizing a modified sugar chain structure of CEAs, and using the amount as an indicator for the detection (Claim 12); A method for detecting a cancer which comprises measuring an amount of a complex of CEAs, an antibody against a common region of CEAs and a protein capable of recognizing a modified sugar chain structure of CEAs, and an amount of a complex of CEAs and the antibody, and using the amount as an indicator for the detection (Claim 13).

Nagata *et al.* teach a method for detecting CEAs comprising using an antibody against a constant region and a protein (lectins) capable of recognizing a modified sugar chain structure of CEAs (abstract). Nagata *et al.* specifically teach a "lectin-linked immunoradiometric assay (L-IRMA) for the simultaneous study of the sugar chain heterogeneity and the quantitative assay of CEA" (page 36, 1st column, 1st paragraph). Nagata *et al.* further teach that the resulting complex of antibody and lectin was specifically detected in a gamma counter (abstract). Nagata *et al.* further teach the detection of cancers (gastric, lung, rectum and uterine carcinomas) comprising an antibody against a constant region and a protein (lectins) capable of recognizing a modified sugar chain structure of CEAs (Table 3, page 38). Although Nagata *et al.* do not specifically teach that the monoclonal antibody used to detect the CEA complex specifically binds to a

"constant region", the specification teaches (page 6, 1st paragraph), that a constant region means a region common to all CEAs in body fluid. Thus, the claimed antibody appears to be the same as taught in the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-4, 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Mach *et al.* (Annals of the NY Acad. Sci., 1975, Vol. 259, pages 389-403).

Mach *et al.* teach a method for detection of carcinoembryonic antigens (CEAs) having a modified sugar chain structure which comprises reacting an antibody against a constant region of CEAs and a protein capable of recognizing a modified sugar chain structure of CEA to give a complex of CEAs wherein the protein is an antibody which is an anti-Lewis type sugar chain antibody wherein the anti-Lewis type sugar chain antibody is an anti-Le^a antibody. Specifically, figure 4, page 394 indicates that a CEA can be detected by both anti-CEA antibody and anti-Le^a. Similarly, Mach *et al.* provide evidence that CEA and blood group antigens are on the same molecule as Figure 7 shows the elution pattern of CEA with percentage of binding by anti-CEA polyclonal antibodies and anti-blood group B antisera. It was further noted by Mach *et al.* that similar results were obtained with CEA V containing $Lewis^a$ antigen (pages 396-397).

Furthermore, Mach *et al.* teach a schematic representation for detection of carcinoembryonic antigens (CEAs) having a modified sugar chain structure which comprises reacting an antibody against a constant region of CEAs and a protein capable of recognizing a modified sugar chain structure of CEA to give a complex of CEAs wherein the protein is an antibody- see Figure 10, page 399.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-7, 11-13, 16, 18-19, are rejected under 35 U.S.C. 103(a) as being unpatentable over Mach *et al.* (Annals of the NY Acad. Sci., 1975, Vol. 259, pages 389-403) in

combination with the teachings of Pompecki *et al.* (Cancer Research, Vol. 41, 1981, pages 1905-1909) and Tannock *et al.* (The Basic Science of Oncology, 2nd Edition, McGraw-Hill, Inc. 1992, pages 201-204)

Mach *et al.* teach as set forth above.

Mach *et al.* do not specifically teach a method of detecting cancer with the assay of Figure 10. Mach *et al.* do not specifically teach using the anti-Le^a antibody with the assay depicted on page 399, Figure 10.

Pompecki *et al.* teach the selective detection of modified sugar chains on CEAs derived from cancers by using lectins or antibodies and that all CEA preparations except the deglycosylated CEA showed binding to anti-Le^a and anti-Le^b antibodies (page 1907, 1st column).

Tannock *et al.* teach the clinical utility of tumor markers such as CEA in evaluating tumor burden and prognosis. For example, studies in patients who have undergone surgery for breast cancer suggest that CEA is an independent predictor of relapse.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the invention was made to detect cancer using the immunoassay depicted by Mach *et al.* because it is well known in the art that detection of CEA in cancer patients can be used as a prognostic indicator since CEA is a well known tumor marker. One would have been motivated to do so because Mach *et al.* specifically design such an assay for detecting CEA and teach that such an assay capable of detecting such types of immune complexes in the serum of tumor-bearing patients would be of great interest (page 398, 2nd paragraph). Furthermore, it would have been obvious to utilize an anti-Le^a antibody in the assay depicted in Figure 10 of Mach *et al.* because

Mach *et al.* teach that their assay is only a model system (page 399). Furthermore, one of ordinary skill in the art could readily discern that that the constant in this system is an antibody to a constant region of CEA while the variables of the model represent secondary antibodies specific for modified sugar chains- such as the anti-B blood group antiserum depicted in the schematic. Hence, since Pompecki *et al.* have demonstrated the successful detection of modified sugar chains on CEAs derived from cancers by using anti-A, anti-B, anti-Le^a , and anti-Le^b (see Table 1, page 1907) antibodies, it would be a minor and obvious variation to use anti-Le^a antibodies in the double antibody model proposed by Mach *et al.* Furthermore, in view of the history of radiolableled assays which have successfully utilized antibodies to assay CEA in cancer patient sera, one of ordinary skill in the art would have a reasonable expectation of success that the model depicted by Mach *et al.* using anti-Le^a antibodies would detect cancer since- individually, both antibodies and or anti-Lewis antibodies have been shown to detect CEA.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
May 16, 2002

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